

## PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1-1461		<b>FOR FURTHER ACTION</b>		See Form PCT/PEA/416
International application No. PCT/EP2004/001208		International filing date (day/month/year) 10.02.2004		Priority date (day/month/year) 13.02.2003
International Patent Classification (IPC) or national classification and IPC A61K31/60, A61K31/519, A61K31/4184, A61P9/00				
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH & CO. KG				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand  11.08.2004		Date of completion of this report  25.02.2005		
Name and mailing address of the International preliminary examining authority:   European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016		Authorized Officer  Leherte, C  Telephone No. +31 70 340-2748  		

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/001208

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

**Description, Pages**

1-7 as originally filed

**Claims, Numbers**

1-6 as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/001208

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
  - ☒ claims Nos. 1-3, 5  
because:
    - ☒ the said international application, or the said claims Nos. 1, 2 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):  
**see separate sheet**
    - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
    - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
    - ☒ no international search report has been established for the said claims Nos. 1, 3, 5 (all partially)
    - ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
      - the written form ☐ has not been furnished
      - ☐ does not comply with the standard
      - the computer readable form ☐ has not been furnished
      - ☐ does not comply with the standard
    - ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
  - ☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/001208

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	1-6
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-6
Industrial applicability (IA)	Yes: Claims	
	No: Claims	see separate sheet

2. Citations and explanations (Rule 70.7):

**see separate sheet**

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**Box No. VI Certain documents cited**

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1. Certain published documents (Rule 70.10)

and /or

2. Non-written disclosures (Rule 70.9)

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)**

International application No.

PCT/EP2004/001208

**Re Item III.**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1) Claims 1 and 2 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

2) Claims 1, 3 and 5 encompass a genus of compounds defined only by their function ("angiotensin II antagonist"), wherein the relationship between the structural features of the members of the genus and said function have not been defined. In the absence of such a relationship either disclosed in the as-filed application or which would have been recognized based upon information readily available to one skilled in the art, the skilled artisan would not know how to make and use compounds that lack structural definition. The fact that one could have assayed a compound of interest using the claimed assays does not overcome this defect since one would have no knowledge beforehand as to whether or not any given compound (other than those that might be particularly disclosed in an application) would fall within the scope of what is claimed. It would require undue experimentation (be an undue burden) to randomly screen undefined compounds for the claimed activity.

The claims cover all combinations of angiotensin II antagonist with dipyridamole and aspirin, whereas the application provides support and/or disclosure within the meaning of Article 6 PCT for only one such combinations, namely: dipyridamole in combination with acetylsalicylic acid and telmisartan.

In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the pharmaceutical composition, containing dipyridamole in combination with acetylsalicylic acid and telmisartan.

No opinion will be given in respect of subject-matter which is not covered by the search report (Rule 66.1(e) PCT).

**INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)**

International application No.

PCT/EP2004/001208

**Re Item V.**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Attention is drawn to the fact that the present statement expressed as to novelty, inventive step and industrial applicability refers only to matter for which an International Search Report has been drawn up (i.e. only for pharmaceutical compositions, containing dipyridamole in combination with acetylsalicylic acid and telmisartan.

**1) INDUSTRIAL APPLICABILITY**

For the assessment of the present claims 1 and 2 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**2) DOCUMENTS USED IN EXAMINATION**

The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1 : WO 01/15673 A

D2 : XP000933411, MEDICAL LETTER ON DRUGS AND THERAPEUTICS, vol. 42, no. 1071, pages 11-12

D3 : XP009033957, REVUE MEDICALE DE LIEGE, vol. 55, no. 10, 2000, pages 957-959

D4 : XP009033969, HEART DRUG, KARGER, vol. 2, no. 2, pages 93-104

Unless indicated otherwise reference is made to the passages considered relevant in the search report.

### 3) INVENTIVE STEP

The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of claim 1-6 does not involve an inventive step in the sense of Article 33(3)PCT.

The problem to be solved by the present application is the provision of a medicament for the prevention of stroke or reducing the risk of stroke.

The solution proposed by the applicant is a medicament containing dipyridamole in combination with acetylsalicylic acid (ASA) and an angiotensin II antagonist,

Documents D1 discloses the use of AT II antagonists in the manufacture of a medicament for the prevention of stroke.

Document D2, D3 and D4 show that Aggrenox(R) (extended-release dipyridamole and aspirin in combination) are used for the prevention of stroke.

The use of a combination of two or more active ingredients with known identical therapeutic use can only be considered as inventive when a surprising effect, an unexpected high synergistic effect or reduced side effects for example, can be assigned in relation to the claimed therapeutic use. In this respect, the present application lacks supportive evidence.